

20th Biology of *Kluyveromyces lactis* workshop

Orsay, France, 7-9 September 2007.

The special 20th *Kluyveromyces* workshop was organised by Monique Bolotin-Fukuhara and Hiroshi Fukuhara, who is the historical founder of this meeting. The Orsay campus was chosen because it is one of the symbolic birth places of the field.

Two facts were noticeable about the audience. Firstly, the increased interest of industry with companies present from pharmaceutical, food and biofuel areas, and, secondly, the active participation of young scientists.

In 2007 a special issue of FEMS Yeast Research ([Vol. 7-5](#), 2007) '*Kluyveromyces*, an emerging model' was published, which was announced during the 2006 workshop in Parma (Italy).

The Orsay meeting was dominated by studies on what may be called "Comparative Functional Genetics". The availability of the genome sequence of *K. lactis* permits a precise analysis of the evolution of its genes by making comparisons with the genomes of other yeast species. Two main facts articulate the various projects: (1) the genome of *K. lactis* is relatively simple because it has not been subjected to the Whole Genome Duplication (WGD) that happened with the *Saccharomyces* branch, and (2) the Carbon/energy/O₂ metabolism is more representative of that of most eukaryotic organisms, when compared to the pathway in *Saccharomyces*, which is strongly oriented towards alcoholic fermentation. Importantly, these two aspects are interdependent. Sequences are widely analysed to understand evolution, but experimental approaches are less frequently used in functional studies, which, in part, may be due to the time needed to perform time consuming and laborious experiments. As a robust and functional data set has accumulated over a long time of research on *Saccharomyces*, the experimental strategies can be designed efficiently by complementarity in *K. lactis* to decrypt the evolutionary mechanisms acting on its genome.

The central field of Carbon/O₂ metabolism was explored in several presentations. The negative transcriptional autoregulation of pyruvate decarboxylase (PDC1), which controls the access to fermentation, proved to be signalled by direct interaction of the enzyme with a transcriptional regulator (M. Micolonghi, Roma, Italy). The key redox equilibrium of the NAD/NADH₂ couple was explored through the glycerol shuttle, and resulted in the discovery of a new specific metabolic pathway. *GUT2*, the gene encoding a key enzyme in the shuttle, was shown to produce two different mRNAs (M. Saliola, Roma, Italy). This last fact is apparently not rare in *K. lactis*, as shown by numerous Northern images presented during the meeting. The mechanisms and biological meaning of this two-product transcriptional regulation, that contrasts with the two-copy system resulting from the WGD in *Saccharomyces*, would be interesting to elucidate. W.G. Bao (Orsay, France) presented a large data set on genes regulated by the availability of O₂, in both *Saccharomyces* and *K. lactis*. The unique copy of the *K. lactis* gene is often duplicated in the *Saccharomyces* genome, in which one copy is expressed under aerobic conditions, and the other during hypoxia. The regulation of the unique *K. lactis* copy was analysed. M. Hnatova (Lyon, France) presented an elegant dissection of the glucose signalling pathway, including loops, ubiquitine impact, transcription factors and sensors. Considering the evolution of each part of the system, in the light of the phylogenetic proximity of each gene with its orthologous copies in

Saccharomyces, permitted a fruitful advance. At the top of the cascade governing the fermentation/respiration shift in *Saccharomyces* is the HAP4 transcriptional activator, governing about 600 genes. The evolutionary history of this gene throughout the yeast kingdom, with *Hansenula polymorpha* as a turning point, proved to be an interplay of domains, in which DNA binding domains are major players. This illustrates how a protein losing this domain can nevertheless keep its regulatory function by acquiring a new property of interaction with other DNA binding proteins (M. Bolotin-Fukuhara, Orsay, France).

Concerning the evolution of transcriptional regulatory proteins, the case of the iron metabolism regulator Aft1 is another paradigm of evolution. Two copies exist in *Saccharomyces*, acting on different set of genes. The unique copy of *K. lactis* is clearly more closely related to Aft1 than to Aft2. Experimental definition of the target genes and DNA binding sequences in *K. lactis* highlighted the link between functional and sequential evolution (P.L. Blaiseau, Paris, France). Finally, the quantitative dissection of the Gal4/1/80 proteins and the unexpected discovery of NADP as part of the regulatory complex opens new insights in the classical Gal model (K. Breunig, Halle, Germany).

Beyond the main research field of Carbon/O₂, a number of interesting systems have been explored from comparative functional genomics perspectives. Among these were the presence of the URE3 prion in *K. lactis* (M. Aigle, Lyon, France), the importance of protein glycosylation for Ca²⁺ homeostasis (E. Zanni, Roma, Italy), the MDR gene family and its regulators (M. Sarinova, Bratislava, Slovak Republic), the surprising behaviour of telomeres (C. Machlitt, Halle, Germany), the APSES regulatory family governing the dimorphism in the phylum of the Ascomycota (A. Dominguez, Salamanca, Spain), and a global study of the *K. lactis* secretome (F. Passos, Vicosa, Brazil).

H. Fukuhara (Orsay, France) ended this stimulating meeting with a clear minded reflection on the future of *K. lactis* in science. He stated that 'a model is not studied for itself, but for a more general field in science'. The workshop has evolved, showing the real importance of *K. lactis* as a model. Comparative functional genomics seems to be the guide line for pursuing this.

In the closure of the workshop, Hiroshi Fukuhara was honoured for his pioneering work in the field. Therefore, the original 2359/152 auxotrophic *Kluyveromyces lactis* strain, which forms the base of all genetic work done on *K. lactis*, was proposed to be renamed HF1987. The next workshop will be organised by M. Wesolowski in Lyon, September 2008.

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